IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT:	Trang T. Le et al.	GROUP ART UNIT:	1615
SERIAL NO.:	09/932,494	CONFIRMATION NO.:	5208
EXAMINER:	Susan T. Tran	ATTORNEY DOCKET NO.:	PC31245
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TITLE: ORAL FAST-MELT FORMULATION OF A CYCLOOXYGENASE-2 INHIBITOR

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

April 17, 2007

AMENDMENT F

Sir:

In response to the Office action of October 17, 2006, the time for response to which has been extended by three months, please enter the following amendments and consider the following remarks.

Amendments to the Claims are reflected in the listing of claims that begins on page 2 of this paper.

Remarks/Arguments begin on page 10 of this paper.

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (currently amended): A process for preparing **[[an]] a solid** oral fast-melt pharmaceutical composition, the process comprising:

(a) a step of wet granulating a drug in an amount of about 15% to about 75% by weight of the composition together with a liquid binding agent comprising a saccharide having high moldability,

(b) a step of blending with the drug a saccharide having low moldability, and

(c) a step of adding a surfactant;

wherein steps (a), (b), and (c) occur in any order or simultaneously to result in formation of granules, wherein the drug has at least one property conferring upon the drug a tendency to agglomerate in the composition, wherein the drug is celecoxib, and wherein said surfactant is selected from the group consisting of quaternary ammonium compounds, dioctyl sodium sulfosuccinate, polyoxyethylene alkylphenyl ethers, polyoxyethylene block copolymers, polyoxypropylene block copolymers, polyoxyethylene fatty acid glycerides, polyoxyethylene fatty acid oils, polyoxyethylene alkyl ethers, polyoxyethylene fatty acid esters, polyoxyethylene sorbitan esters, propylene glycol fatty acid esters, sodium lauryl sulfate, fatty acids, salts of fatty acids, glyceryl fatty acid esters, sorbitan esters, tyloxapol, and mixtures thereof.

Claim 2 (original): The process of Claim 1 wherein said step (b) occurs prior to or simultaneously with said step (a).

Claim 3 (original): The process of Claim 1 wherein said wet granulating step comprises fluid bed granulation.

Claims 4-9 (cancelled).

Claim 10 (original): The process of Claim 1 wherein said saccharide having low moldability is selected from the group consisting of lactose, mannitol, glucose, sucrose and xylitol.

Claim 11 (original): The process of Claim 1 wherein said saccharide having low moldability is mannitol of powder grade.

Claim 12 (original): The process of Claim 1 wherein said saccharide having high moldability is selected from the group consisting of maltose, maltitol, sorbitol and oligosaccharides having 2 to 6 monosaccharide residues.

Claim 13 (original): The process of Claim 1 wherein said saccharide having high moldability is maltose.

Claims 14-17 (cancelled).

Claim 18 (previously presented): The process of Claim 1 wherein said surfactant is added in a total amount of about 0.05% to about 5% by weight of the composition.

Claim 19 (previously presented): The process of Claim 1 wherein said surfactant is added in a total amount of about 0.075% to about 2.5% by weight of the composition.

Claim 20 (previously presented): The process of Claim 1 wherein said surfactant is added in a total amount of about 0.25% to about 1% by weight of the composition.

Claim 21 (previously presented): The process of Claim 1 wherein step (c) further comprises addition of at least one glidant.

Claim 22 (previously presented): The process of Claim 21 wherein said at least one glidant is silicon dioxide and/or talc.

Claim 23 (previously presented): The process of Claim 21 wherein said at least one glidant is added in a total amount of about 0.05% to about 5% by weight of the composition.

Claim 24 (previously presented): The process of Claim 21 wherein said at least one glidant is added in a total amount of about 0.1% to about 2% by weight of the composition.

Claim 25 (previously presented): The process of Claim 21 wherein said at least one glidant is added in a total amount of about 0.25% to about 1% by weight of the composition.

Claims 26-27 (cancelled).

Claim 28 (previously presented): The process of Claim 1 wherein said drug is present in an amount of about 30% to about 75% by weight of the composition.

Claim 29 (previously presented): The process of Claim 1 wherein said drug is present in an amount of about 45% to about 75% by weight of the composition.

Claim 30 (original): The process of Claim 1 wherein said saccharide having high moldability is present in a total amount of about 1% to about 10% by weight of the composition.

Claim 31 (original): The process of Claim 1 wherein said saccharide having high moldability is present in a total amount of about 1% to about 7.5% by weight of the composition.

Claim 32 (original): The process of Claim 1 wherein said saccharide having high moldability is present in a total amount of about 1% to about 5% by weight of the composition.

Claim 33 (original): The process of Claim 1 wherein said saccharide having low moldability is present in a total amount of about 10% to about 90% by weight of the composition.

Claim 34 (original): The process of Claim 1 wherein said saccharide having low moldability is present in a total amount of about 15% to about 60% by weight of the composition.

Claim 35 (original): The process of Claim 1 wherein said saccharide having low moldability is present in a total amount of about 25% to about 50% by weight of the composition.

Claim 36 (original): The process of Claim 1 wherein the weight ratio of said saccharide having high moldability to said saccharide having low moldability is about 2:100 to about 20:100.

Claim 37 (original): The process of Claim 1 wherein the weight ratio of said saccharide having high moldability to said saccharide having low moldability is about 5:100 to about 10:100.

Claim 38 (original): The process of Claim 1 wherein the weight ratio of said saccharide having high moldability to said saccharide having low moldability is about 5:100 to about 7.5:100.

Claim 39 (previously presented): The process of Claim 1, further comprising

(d) a step of blending said granules with at least one of a lubricant, a sweetening agent and a flavoring agent to form a tableting blend, and

(e) a step of compressing the tableting blend to form oral fast-melt tablets.

Claim 40 (previously presented): The process of Claim 39 wherein parameters are set in said compressing step (e) to provide tablets having a hardness of about 1 to about 10 kp.

Claim 41 (previously presented): An oral fast-melt pharmaceutical composition prepared by the process of any of Claims 1-3, 10-13, 18-25, and 28-40.

Claims 42-45 (cancelled).

Claim 46 (currently amended): The composition of Claim **[[99]] 41** wherein said surfactant is present in an amount of about 0.05% to about 5% by weight of the composition.

Claim 47 (currently amended): The composition of Claim **[[99]] 41** wherein said surfactant is present in an amount of about 0.075% to about 2.5% by weight of the composition.

Claim 48 (currently amended): The composition of Claim **[[99]] 41** wherein said surfactant is present in an amount of about 0.25% to about 1% by weight of the composition.

Claim 49 (cancelled).

Claim 50 (previously presented): The composition of Claim 96 wherein said glidant is silicon dioxide and/or talc.

Claim 51 (previously presented): The composition of Claim 50 wherein said glidant is present in an amount of about 0.05% to about 5%.

Claim 52 (previously presented): The composition of Claim 50 wherein said glidant is present in an amount of about 0.1% to about 2%.

Claim 53 (previously presented): The composition of Claim 50 wherein said glidant is present in an amount of about 0.25% to about 1%.

Claims 54-61 (cancelled).

Claim 62 (currently amended): The composition of Claim **[[99]] 41** wherein said drug is present in an amount of about 30% to about 75% by weight of the composition.

Claim 63 (currently amended): The composition of Claim **[[99]] 41** wherein said drug is present in an amount of about 45% to about 75% by weight of the composition.

Claim 64 (currently amended): The composition of Claim **[[99]] 41** wherein said saccharide having low moldability is selected from lactose, mannitol, glucose, sucrose and xylitol.

Claim 65 (currently amended): The composition of Claim **[[99]] 41** wherein said saccharide having low moldability is present in an amount of about 10% to about 90% by weight of the composition.

Claim 66 (currently amended): The composition of Claim **[[99]] 41** wherein said saccharide having low moldability is present in an amount of about 15% to about 60% by weight of the composition.

Claim 67 (currently amended): The composition of Claim **[[99]] 41** wherein said saccharide having low moldability is present in an amount of about 25% to about 50% by weight of the composition.

Claim 68 (currently amended): The composition of Claim **[[99]]** **41** wherein said saccharide having low moldability is mannitol of powder grade.

Claim 69 (currently amended): The composition of Claim **[[99]]** **41** wherein said saccharide having high moldability is selected from the group consisting of maltose, maltitol, sorbitol and oligosaccharides having 2 to 6 monosaccharide residues.

Claim 70 (currently amended): The composition of Claim **[[99]]** **41** wherein said saccharide having high moldability is maltose.

Claim 71 (currently amended): The composition of Claim **[[99]]** **41** wherein said saccharide having high moldability is present in an amount of about 1% to about 10% by weight of the composition.

Claim 72 (currently amended): The composition of Claim **[[99]]** **41** wherein said saccharide having high moldability is present in an amount of about 1% to about 7.5% by weight of the composition.

Claim 73 (currently amended): The composition of Claim **[[99]]** **41** wherein said saccharide having high moldability is present in an amount of about 1% to about 5% by weight of the composition.

Claim 74 (currently amended): The composition of Claim **[[99]]** **41** wherein the weight ratio of said saccharide having high moldability to said saccharide having low moldability is about 2:100 to about 20:100.

Claim 75 (currently amended): The composition of Claim **[[99]]** **41** wherein the weight ratio of said saccharide having high moldability to said saccharide having low moldability is about 5:100 to about 10:100.

Claim 76 (currently amended): The composition of Claim **[[99]]** **41** wherein the weight ratio of said saccharide having high moldability to said saccharide having low moldability is about 5:100 to about 7.5:100.

Claim 77 (currently amended): The composition of Claim **[[99]]** **41** that is in the form of a tablet.

Claim 78 (previously presented): The composition of Claim 77 wherein said tablet disintegrates within about 30 to about 300 seconds in a standard in vitro disintegration assay.

Claim 79 (previously presented): The composition of Claim 77 wherein said tablet disintegrates within about 30 to about 200 seconds in a standard in vitro disintegration assay.

Claim 80 (previously presented): The composition of Claim 77 wherein said tablet disintegrates within about 30 to about 150 seconds in a standard in vitro disintegration assay.

Claim 81 (previously presented): The composition of Claim 77 wherein said tablet disintegrates within about 5 to about 60 seconds after placement in the oral cavity of a subject.

Claim 82 (previously presented): The composition of Claim 77 wherein said tablet disintegrates within about 5 to about 30 seconds after placement in the oral cavity of a subject.

Claim 83 (previously presented): The composition of Claim 77 wherein said tablet disintegrates within about 5 to about 25 seconds after placement in the oral cavity of a subject.

Claims 84-85 (cancelled).

Claim 86 (currently amended): A method of treating a medical condition or disorder in a mammalian subject where treatment with a cyclooxygenase-2 inhibitor is indicated, comprising orally administering to the subject a composition of Claim **[[99]]** **41**.

Claim 87 (original): The method of Claim 86 wherein said mammalian subject is a human subject.

Claim 88 (original): The method of Claim 87 that further comprises combination therapy with one or more drugs selected from the group consisting of opioids and other analgesics.

Claim 89 (original): The method of Claim 87 that further comprises combination therapy with an opioid compound selected from the group consisting of codeine, meperidine, morphine and derivatives thereof.

Claims 90-94 (cancelled).

Claim 95 (previously presented): The process of Claim 1 where the at least one surfactant comprises sodium lauryl sulfate.

Claim 96 (currently amended): The composition of Claim **[[99]]** **41** further comprising at least one glidant.

Claim 97 (previously presented): The process of Claim 1 wherein the drug is dispersed in the composition.

Claim 98 (previously presented): The process of Claim 1 wherein said at least one property is selected from the group consisting of electrostatic, cohesive, low bulk density, low compressibility, and poor flow.

Claims 99-102 (cancelled).

REMARKS

Status of the claims

Claims 1-3, 10-13, 21, 22, 28-41, 46-48, 50-53, 62-83, 86-89, and 96-100 are currently pending. All pending claims stand rejected under 35 U.S.C. §103(a) as being unpatentable over Mizumoto et al., U.S. Patent No. 5,576,014 ("Mizumoto") in view of Love, U.S. 6,573,290 ("Love") or Straub et al., U.S. 6,395,300 ("Straub").

Claims 1-3, 10-13, 18-25, 28-41, 46-48, 50-53, 62-83, 86-89, and 95-100 stand rejected under §103(a) as being unpatentable over Mizumoto in view of Love or Straub and Jain et al., U.S. Patent No. 6,316,029 ("Jain").

Claims 99 and 100 have been cancelled.

Claim 1 has been amended to specify that the oral fast-melt pharmaceutical composition is a solid composition. Support for this amendment may be found, for example, at page 9, lines 6-9 of the instant specification.

Claims 46-48, 62-77, 86, and 96 have been amended to depend from claim 41.

Mizumoto in view of Love or Straub

Reconsideration is respectfully requested of the rejection of claims 1-3, 10-13, 21, 22, 28-41, 46-48, 50-53, 62-83, 86-89, and 96-100 under §103(a) as being unpatentable over Mizumoto in view of Love or Straub. Applicants respectfully repeat their assertion that the Office has not shown that claims 1-3, 10-13, 21, 22, 28-41, 46-48, 50-53, 62-83, 86-89, and 96-100 are *prima facie* obvious over Mizumoto in view of Love or Straub.

Claim 1 requires a step of adding a surfactant selected from the group consisting of quaternary ammonium compounds, dioctyl sodium sulfosuccinate, polyoxyethylene alkylphenyl ethers, polyoxyethylene block copolymers, polyoxypropylene block copolymers, polyoxyethylene fatty acid glycerides, polyoxyethylene fatty acid oils, polyoxyethylene alkyl ethers, polyoxyethylene fatty acid esters, polyoxyethylene sorbitan esters, propylene glycol fatty acid esters, sodium lauryl sulfate, fatty acids, salts of fatty acids, glyceryl fatty acid esters, sorbitan esters, tyloxapol, and mixtures thereof.

A *prima facie* showing of obviousness requires, *inter alia*, that the prior art references teach or suggest all the claim limitations. See MPEP §2143. Claim 1 requires addition of a surfactant selected from the group shown above. Mizumoto is silent as to these surfactants. Love mentions that *solutions* of therapeutic compositions described therein "may be prepared in water mixed with a surfactant, such as hydroxypropylcellulose." See col. 11, lines 29-31. Love does not mention any

of the surfactants named above, nor does Love describe a solid fast-melt composition comprising one of these surfactants, as required by claim 1. The combination of Mizumoto and Love does not describe or suggest all the limitations of claim 1 or of the claims depending therefrom. Thus, the Office has not shown that claims 1-3, 10-13, 21, 22, 28-41, 46-48, 50-53, 62-83, 86-89, and 96-100 are *prima facie* obvious in view of Mizumoto and Love.

Straub describes formulations of low solubility drugs in a porous matrix wherein the dissolution rate of the drug is enhanced when the matrix is contacted with an aqueous medium. Straub names at least 45 categories of drugs (see col. 4, line 22 through col. 7, line 20) contemplated for use in his compositions. Over 410 drugs are identified by name; one of these is celecoxib. Straub names over 100 drugs as preferred (see col. 7, line 45 through col. 8, line 9). Celecoxib is one of these drugs. As previously mentioned, Straub does not described any specific composition comprising celecoxib, and there is no indication whatsoever in Straub that celecoxib is particularly preferred. Furthermore, Straub does not specifically teach processing celecoxib with an excipient such as a wetting agent or surfactant. Rather, Straub mentions that wetting agents may in general be used to facilitate dissolution, but **does not describe the specific combination of celecoxib with a wetting agent or surfactant**. Thus, the combination of Mizumoto and Straub does not describe or suggest all the limitations of claim 1 or of the claims depending therefrom. Thus, the Office has not shown that claims 1-3, 10-13, 21, 22, 28-41, 46-48, 50-53, 62-83, 86-89, and 96-100 are *prima facie* obvious in view of Mizumoto and Straub.

Mizumoto in view of Love or Straub and Jain

Reconsideration is respectfully requested of the rejection of claims 1-3, 10-13, 18-25, 28-41, 46-48, 50-53, 62-83, 86-89, and 95-100 under §103(a) as being unpatentable over Mizumoto in view of Love or Straub and Jain. Applicants respectfully repeat their assertion that the Office has not shown that claims 1-3, 10-13, 18-25, 28-41, 46-48, 50-53, 62-83, 86-89, and 95-100 are *prima facie* obvious over Mizumoto in view of Love or Straub and Jain.

Jain describes rapidly disintegrating or dissolving solid dose formulations of nanoparticulate compositions comprising a poorly soluble nanoparticulate drug or other agent having an effective average particle size of less than about 2000 nm and a surface stabilizer adsorbed on the surface thereon. As described by Jain, the "surface stabilizer is absorbed on the surface of the active agent in an amount sufficient to maintain an effective average particle size of less than about 2000 nm for the active agent." See col. 7, lines 21-24.

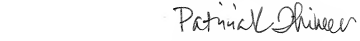
Nothing in Jain suggests the need for formulating their poorly soluble drug and surface stabilizer with the saccharide having low moldability and the saccharide having high moldability

required by Mizumoto. Jain's nanoparticulate compositions, and Mizumoto's intrabuccally dissolving compressed moldings comprising granules comprising a saccharide having low moldability and a saccharide having high moldability, would, at the very most, be seen as alternatives to one another, which one skilled in the art would have no reason or motivation to combine. Neither Love nor Straub provide this motivation. Love mentions surfactants only with respect to solutions, and Straub provides no reason or motivation to select celecoxib from the over 400 drugs described therein. Thus, the combination of Mizumoto with Love or Straub and Jain does not describe or suggest all the limitations of claim 1 or of the claims depending therefrom. Thus, the Office has not shown that claims 1-3, 10-13, 18-25, 28-41, 46-48, 50-53, 62-83, 86-89, and 95-100 are *prima facie* obvious in view of Mizumoto and Straub.

Conclusion

For the foregoing reasons, the Applicants submit that the present invention is now in condition for allowance. Allowance of all pending claims is respectfully solicited.

Respectfully submitted,



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